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REMARKS

The present application was originally filed with 29 Claims. In a Restriction Requirement mailed November 18, 2003, the Examiner restricted the Claims into 12 Groups:

Group I: Claims 1-4, 17, 28, and 29, drawn to a cutinase variant having a substitution of Gly at position 59 of SEQ ID NO:2;

Group II: Claims 1-3, 5, 24, 28, and 29, drawn to a cutinase variant having a substitution of Thr at position 177 of SEQ ID NO:2;

Group III: Claims 1-3, 6, 25, 28, and 29, drawn to a cutinase variant having a substitution of Thr at position 64 of SEQ ID NO:2;

Group IV: Claims 1-3, 7, 28, and 29, drawn to a cutinase variant having a substitution of Tyr at position 150 of SEQ ID NO:2;

Group V: Claims 1-3, 8, 26, 28, and 29, drawn to a cutinase variant having a substitution of Tyr at position 182 of SEQ ID NO:2;

Group VI: Claims 1-3, 9-10, 12-16, 19, and 27-29, drawn to a cutinase variant having a substitution of Phe at position 180, Ser at position 205, and Ile at position 178 of SEQ ID NO:2;

Group VII: Claims 1-3, 11, 28, and 29, drawn to a cutinase variant having a substitution of Gly at position 61 of SEQ ID NO:2;

Group IX: Claims 1-3, 20, 28, and 29, drawn to a cutinase variant having a substitution of Arg at position 20, and Tyr at position 112 of SEQ ID NO:2;

Group X: Claims 1-3, 21, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 205 and Phe at position 207 of SEQ ID NO:2;

Group XI: Claims 1-3, 22, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 63 of SEQ ID NO:2; and

Group XII: Claims 1-3, 23, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 85 of SEQ ID NO:2

The Examiner argued that the Groups represent separate and patentably distinct inventions. In a Response filed December 16, 2003, Applicants respectfully traversed the restriction requirement and elected the Claims in Group VI (Claims 1-3, 9-10, 12-16, 19, and 27-29, drawn to a cutinase variant having a substitution of Phe at position 180, Ser at position 205, and Ile at position 178 of SEQ ID NO:2). Applicants withdrew Claims 4-8, 11, 17-18, and 20-26, as being drawn to a non-elected invention. In the present Office Action, the Examiner

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has made the Restriction final. In the present Response, Applicants have cancelled Claims 4-8, 17-18, and 20-26. Applicants reserve the right to pursue these and/or similar Claims in one or more Divisional and/or other application. In order to avoid any additional confusion, Applicants have also cancelled Claims 12-16, in order to correct the inadvertent omission of Claim 12 in the Response filed December 12, 2003. New Claims 34-38 correspond to Claims 12-16 with amendments to correct sentence structure. There is no new matter in the presently added Claims. Applicants address the Examiner's rejections of Claims 12-16 as they pertain to new Claims 34-38. New Claims 30 and 31 are added to recite an additional substitution at position 219 of SEQ ID NO:2, in addition to the substitutions at positions 192 and 194, as recited in amended Claims 1 and 28. New Claim 32 has been added to recite the enhanced thermostability of the cutinase of Claim 31. Applicants note that Claim 10 has been cancelled and corresponding Claim 33 has been added. No new matter is added in these amendments nor in the new Claims.

The Examiner has indicated that the Title is not descriptive and has suggested a new Title. Applicants appreciate the Examiner's suggestion and have amended the Title. In addition, Applicants have amended Table 1 and the text in the Specification that refers to the color-coding of Table 1. Furthermore, Applicants have corrected the use of trademarks in the Specification. No new matter is added by any of these amendments.

The Examiner has objected to Claims 10 and 14 for the recitation of "Glyc" (Claim 10) and "Phy 180" (Claim 14). In addition, the Examiner has objected to Claim 13 for using the full amino acid name for "leucine," rather than the three-letter abbreviated version used in every other Claim. Applicants have amended the Claims appropriately and thank the Examiner for his suggestions.

The Examiner's rejections are addressed below in the following order:

- 1) Claims 2-3, 9-10, 12-15, 19 and 27-29, stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite;
- 2) Claims 1-3, 9-10, 12-15, 19, and 27-29, stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 3) Claims 1-3, 9-10, 12-15, 19, and 27-29 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled;
- 4) Claims 1-3, 9, 12, and 28-29, stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Poulouse *et al.* (US Pat. No. 5,352,594), as evidenced by Boston *et al.* (Meth. Enzymol., 284:298-317); and

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5) Claims 10-13-15, and 27, stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Poulouse *et al.*

1) The Claims are Definite

The Examiner has rejected Claims 2-3, 9-10, 12-15, 19 and 27-29, under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants must respectfully disagree.

In regard to Claims 2 and 29, the Examiner argues that the recitation of "derived from" is indefinite. In order to more clearly recite the claimed invention, Applicants have amended these Claims to recite "isolated from." The Examiner has also rejected Claim 3 as being confusing regarding SEQ NO.2 and the recitation of variants. In order to more clearly recite the claimed invention, Applicants have cancelled Claim 3 without prejudice. These amendments find more than sufficient support in the Specification and no new matter has been added. Applicants respectfully submit that these Claims are definite and request that these rejections be withdrawn.

The Examiner argues that Claims 9 and 27 are indefinite in the recitation of "stability." In addition, the Examiner argues that the term "enhanced stability," in Claims 9 and 27; "enhanced polyesterase activity in Claims 12-15 and 19; and "thermostable" in Claim 28 are unclear without a statement defining to what these properties are being compared. While Applicants believe that the Claims are definite, the Claims have been amended to recite that the properties are "enhanced" as compared to wild-type enzyme. New Claims 32, and 34-38 also include the comparative language. However, in regards to Claim 27, there is no comparative language. Thus, as the term "thermostable" is known to those in the art, this Claim has not been amended. These amendments find more than sufficient support in the Specification and no new matter has been added. Applicants respectfully submit that these Claims are definite and request that these rejections be withdrawn.

The Examiner further argues that Claim 10 is indefinite in the recitation of "Phe is substituted" and "Ser is substituted." The Examiner argues that it is unclear which of the different Phe and Ser residues in SEQ ID NO:2 are involved. Although Claim 10 has been cancelled and this rejection is therefore moot, Applicants note that new Claim 33 recites that the Phe is the Phe residue at position 194 and the Ser is the Ser residue at position 219. These amendments find more than sufficient support in the Specification and no new matter has been added. Applicants respectfully submit that Claim 33 is definite and request that this rejection be withdrawn.

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The Examiner also argues that Claims 13-15, 19, and 27 are confusing in that the Claims identify residues of SEQ ID NO:2 that are to be mutated, but the amino acid sequence of SEQ ID NO:2 and Figure 18 do not correspond with residue positions recited in the Claims. Applicants note that SEQ ID NO:2 contains a leader peptide and is numbered beginning at the initiating methionine. The mature sequence, after cleavage of the leader peptide (14 amino acid residues) begins at the alanine in position 15 (*i.e.*, Ala 15 represents the first residue in the protein). Therefore, Phe 180 in the Claims refers to Phe 194 in Figure 18 and SEQ ID NO:2. Thus, the Examiner is correct in his assumptions regarding the numbering. In view of this, Applicants have amended the Claims to recite Phe 194 and Ser 219, which correspond to Phe 180 and Ser 205, respectively, in the text and Claims as originally filed. If the Examiner would find a substitute Sequence Listing to be helpful, Applicants would be happy to provide a new Sequence Listing that includes a sequence that omits the leader peptide.

The Examiner has also argued that Claim 27 is confusing in the recitation of "substitution of Phe 180 with one of Ile, Leu, Asn, and Pro." Applicants have amended this Claim to more clearly recite the claimed invention. As the Claim is definite, Applicants respectfully request that this rejection be withdrawn.

2) The Written Description is Met

The Examiner has rejected Claims 1-3, 9-10, 12-15, 19, and 27-29, under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement. In particular, the Examiner argues that "the disclosure of the representative species of SEQ ID NO:2 with amino acid substitution at positions consisting of 178, 180, and 205 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of claimed cutinase variants." (Office Action, page 9).

Applicants must respectfully disagree with the Examiner's arguments, as Applicants have clearly disclosed additional species of cutinase variants, as indicated by the data provided in Table 1 (page 14). In this Table, data for polyesterase activity and thermostability of numerous cutinase variants are provided. Thus, Applicants have provided numerous cutinase variants. Indeed, in Table 14 alone, data are provided for cutinase variants with substitutions at 41 different positions. In view of this, Applicants respectfully submit that there are many more representative species provided in the Specification as filed than the Examiner has recognized. Thus, Applicants respectfully submit that the written description requirement is met and request that this rejection be withdrawn.

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3) The Claims are Enabled

The Examiner has rejected Claims 1-3, 9-10, 12-15, 19, and 27-29, under 35 U.S.C. §112, first paragraph, as allegedly not being enabled. The Examiner admits that the Specification is enabling for SEQ ID NO:2 with substitutions at positions 178, 180, and 205. However, the Examiner argues that the Specification does not provide enablement for other substitutions and homologous variants. As indicated above, Applicants must respectfully disagree, as many more cutinase variants are indeed provided by the Specification as filed (See, Table 1). Thus, in contrast to the Examiner's assertions, the present Specification enables many cutinase variants in addition to those specifically recited in the Claims as having substitutions at positions 178, 180 and 205 (*i.e.*, 192, 194 and 219) of SEQ ID NO:2. Nonetheless, in order to further Applicants' business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have amended the Claims to remove the recitation of homologues. Applicants explicitly reserve the right to pursue the originally filed, as well as additional Claims in one or more further applications. As the Claims are enabled, Applicants respectfully request that this rejection be withdrawn.

4) The Claims are Novel

The Examiner has rejected Claims 1-3, 9, 12, and 28-29, under 35 U.S.C. §102(b), as allegedly being anticipated by Poulouze *et al.* (US Pat. No. 5,352,594), as evidenced by Boston *et al.* (Meth. Enzymol., 284:298-317). In particular, the Examiner argues that Poulouze *et al.* teach variants of a *P. mendocina* lipase having substitution of Ser 205 with various amino acids. While Applicants respectfully submit that the presently claimed invention is not anticipated by Poulouze *et al.*, in order to further their business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have amended the Claims such that substitutions at position 219 occur in combination with substitutions at positions 192 and/or 194. As Poulouze *et al.* do not teach nor suggest such combinations, Applicants respectfully submit that the presently claimed cutinase variants are novel over Poulouze *et al.* Thus, Applicants respectfully submit that this rejection be withdrawn.

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5) The Claims are Unobvious

The Examiner has rejected Claims 10-13-15, and 27, under 35 U.S.C. §103(a) as allegedly being unpatentable over Poulouse *et al.* In particular, the Examiner argues that "Poulouse *et al.* teach that in order to obtain an enzyme with the best ratio or substrate specificity in a desired direction, more than one amino acid substitution can be made" (Office Action, page 15). The Examiner concludes that it would have been obvious to mutate position 180 of *P. mendocina* lipase or to further mutate position 180 of the *P. mendocina* lipase position 205 mutants of Poulouse *et al.* with any amino acid." (Office Action, page 16). Applicants must respectfully disagree with the Examiner's arguments.

Applicants also note that the Examiner admits that "Poulouse *et al.* do not teach that their *P. mendocina* esterase Ser205 variants have enhanced stability or enhanced polyesterase activity." (Office Action, page 16). The Examiner indicates that Applicants have the burden of showing a novel or unobvious difference between the claimed product and the product of the prior art . . ." (Office Action, page 16). During the development of the presently claimed invention, Applicants conducted experiments using the best-performing variants as described by Poulouse *et al.* (*i.e.*, S205N, Q127S/S205N, and S205N/F207T) to determine their polyesterase activity. The activity of these variants was found to be unremarkable, as compared to the wild-type cutinase. As the teachings of Poulouse *et al.* were insufficient to meet the need addressed in the present application (*i.e.*, variants with enhanced thermostability and/or polyesterase activity), the present inventors developed the presently claimed invention in order to provide cutinase mutants with these desired properties. Should the Examiner wish to review these data, Applicants will provide them upon request.

As the presently claimed invention is neither taught, suggested, nor is there any expectation of success in producing the presently claimed invention provided in Poulouse *et al.*, Applicants respectfully submit that the presently claimed invention is unobvious over Poulouse *et al.* Therefore, Applicants respectfully request that this rejection be withdrawn.


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CONCLUSION

In view of the above remarks, the Applicants believe the pending Claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

Date: July 15, 2004


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